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THE ASSAY OF IODOFORM AND IODOFORM GAUZE.

By A. H. Clark.

In searching the available literature for a satisfactory method for the determination of iodoform in medicated gauze and also for the assay of iodoform, the method of Uts (*Apoth. Ztg.*, 18, No. 98, Dec. 9, 1903, 869) and that of Gane and Webster (*Merck's Report*, 18, No. 1, p. 13, 1909) seemed to be the most readily applicable.

Uts dissolves the iodoform in spirit of ether, adds fuming nitric acid, an excess silver nitrate V.S., and heats until the odor of nitrous acid has disappeared. The excess of silver nitrate V.S. is then determined with $^1/_{10}$ normal ammonium sulphocyanide V.S.

Gane and Webster dissolve the iodoform in alcohol and ether in the proportion of 3 parts of alcohol to 1 part of ether. Commercial nitrous acid is then added, the mixture heated, and the excess silver nitrate V.S. determined with $^1/_{10}$ normal potassium sulphocyanide V.S. Gauze, lint, etc., are exhausted with ether and the ethereal solution treated as described.

Both methods were found to give excellent satisfaction. In the effort to shorten the method as applied to gauze, I found that it is not necessary to *dissolve* the iodoform in alcohol or ether, neither is the *fuming* nitric acid necessary. Boiling under a reflux condenser for one-half hour in the presence of alcohol and nitric acid, U.S.P., is sufficient to convert all of the iodine to silver iodide. By the use of alcohol alone a simultaneous extraction of the gauze and determination of the iodoform may be carried out, and this much easier than if ether is present. Using ether for

extraction with water present, the temperature of the distilling flask must be carefully controlled or it will rise to such a point that when the ether siphons over and comes in contact with the hot water it will vaporize so rapidly that there is great danger of loss. There is no trouble of this kind if alcohol only is used. The following is the process in detail as finally adapted to the assay of iodoform.

The iodoform is added to 50 c.c. $^1/_{10}$ normal silver nitrate V.S., to which has been added 3 c.c. nitric acid, U.S.P., 50 c.c. alcohol is added, the whole being contained in a 250 c.c. florence flask. The flask is now connected with a reflux condenser and heat applied so that it boils gently. The heating is best conducted by placing the flask in a water-bath so that the water in the bath is about on a level with the water in the flask. This procedure avoids any bumping or spattering. The heat is continued for one-half hour after the boiling commences. After allowing the flask to cool, water is added to make about 150 c.c., a little ferric ammonium sulphate T.S. added, and the excess silver nitrate V.S. determined with potassium sulphocyanide V.S. Each c.c. $^1/_{10}$ normal silver nitrate V.S. is equivalent to 0.0130 Gm. iodoform. The following experiments demonstrate the accuracy of the method.

A sample of iodoform was first procured of good quality and its purity determined by the Carius method. This sample was used in all of the experiments recorded below.

Iodoform taken.	Silver iodide weighed.	Iodoform found.	Per cent. pure.
0.7011	1.2631	0.7048	100.52
0.5352	0.9632	0.5382	100.56

The sample was then assayed by the method as given above.

Iodoform taken.	Iodoform found.	Per cent. pure.
0.3375	0.3386	100.33
0.2011	0.2017	100.29
0.1814	0.1819	100.27
0.2094	0.2095	100.05

The principle is applied to the assay of gauze as follows:

The gauze is placed in a Soxhlet extractor of about 60 c.c. capacity and the entire apparatus connected as usual, except that a

250 c.c. florence flask, containing the $^1/_{10}$ normal silver nitrate V.S. and the nitric acid, is connected with the extraction tube in place of the usual wide-mouth extraction flask. A water-bath is placed so that the flask is immersed in the water as described above. Alcohol is then poured through the condenser onto the gauze in the extraction tube until it siphons into the flask. Heat is then applied to the water-bath until the contents of the flask boil briskly. The extraction is continued for one hour, when the flask is disconnected and, after cooling, the titration made as described above. Experiments were made in which a known weight of iodoform was added to plain gauze and treated as above described. The results follow:

Iodoform taken.	Iodoform found.	Per cent. found.
0.2111	0.2117	100.29
0.1953	0.1952	99.95
0.4336	0.4355	100.45

The method is, of course, open to the objection that in commercial gauze the alcohol might extract substances other than iodoform which will consume the silver nitrate solution, and thus make the result too high. The absence of such substances would have to be demonstrated before the assay is made. The method has given perfect satisfaction in a large number of determinations where the absence of interfering substances was known.

University of Illinois School of Pharmacy.

PHYSIOLOGIC STANDARDIZATION OF CARDIAC STIMULANTS AND DEPRESSANTS.

By Thomas S. Githens, M.D.

TOGETHER WITH A COMPARISON OF SUCH STANDARDIZATION WITH SOME RESULTS OBTAINED BY CHEMICAL ASSAY.

By Charles E. Vanderkleed, Phar. D.

In spite of the large amount of physiologic work which has been done with the vegetable drugs in order to determine the method by which they act and the organs and processes which are first and most markedly affected, we find very little in the literature in regard to determination of the strength of these drugs or the

amount required to produce certain effects. In the text-books on therapeutics we find a distinction drawn between the effects of "small" and of "large" or "toxic" doses on the various animals used for experimental purposes, but very rarely do we find any exact statement as to what amount of the drug per gramme of animal constitutes such a dose.

For this reason it has seemed interesting as well as important to determine the exact amount of various drugs which was required to produce definite effects in laboratory animals and to determine also which method of testing was best suited to each drug.

Commercially this study is of importance on account of the desire of manufacturers of these drugs and their products to put on the market preparations of definite physiologic strength, from drugs the chemical study of which is not a criterion of activity. My studies have been largely limited to such drugs for this reason.

The drugs whose standardization I will consider are apocynum, aconite, convallaria, digitalis, gelsemium, squill, strophanthus, and veratrum. These drugs fall into two groups: those which raise blood-pressure, the so-called digitalis series, apocynum, convallaria, digitalis, squill, and strophanthus; and those which lower blood-pressure, aconite, gelsemium, and veratrum.

We will consider, first, the drugs of the digitalis series. Three methods are available for the purpose of quantitative determination of their activity.

1. The effect on the isolated heart of the frog or turtle.
2. The effect on the blood-pressure.
3. The amount required to cause death.

As the effect on the heart is that which makes these drugs useful in practical medicine, it is often stated that the best method of testing them is directly on the heart. The effect on this organ can be studied to the exclusion of all other factors by the following method: The heart of a frog or turtle will continue to beat, if it is placed in a solution of proper salts, after its removal from the body. If the heart is cut into longitudinal strips, each of these will continue to beat under proper conditions, and may live for two or even three days after removal from the body. It would seem that by adding the drug to be tested to the liquid in which the strips are suspended, the effect of this on the heart itself might be determined with great accuracy. This would be true

but for the fact that organs isolated from the body and kept under artificial conditions are very susceptible to slight alterations in their surroundings,—so much so, that if four strips are cut from the same heart and are kept under apparently identical conditions, they may show great differences among themselves, and although the effect of the addition of a given drug to the solution might easily be seen in the alteration of the rhythm, the differences between the reaction of different strips would be greater than that between different specimens of the same drug. In work of this sort which I have done, I found that the difference in the effect of a given quantity of a drug and twice this amount was not very marked, although there was generally a fairly marked difference between a given amount and four times as much. A method which gives results showing a variation of 50 per cent. in one direction or the other can of course not be depended on for quantitative standardization.

The second method, the effect on the blood-pressure, has also something in its favor, inasmuch as the stimulating effect of these drugs on the heart is in more or less direct proportion to the effect on the blood-pressure. If the effect of drugs on the blood-pressure is studied, it will be found that the rise following an injection is not in proportion to the dose given. A small dose will cause a perceptible rise, but twice this dose will not cause twice this rise. In fact, we find that a certain dose brings about almost a maximal rise and that increasing the dose will merely increase toxic phenomena, so that the pressure will fall more rapidly than after the smaller dose. The effects of large and small doses are thus distinguished with difficulty and the same is, *pari passu,* true of equal doses of strong and weak preparations. It is evident from these facts that if we choose as our standard dose the smallest amount which will bring about a maximum rise, a drug much stronger than our standard will cause much the same rise and will, through its toxic action, cause the pressure to fall sooner than would a weaker preparation, and thus a strong preparation will appear weak instead of strong.

To avoid this tendency to toxic action it will be necessary to give a dose, of the preparation to be tested, so small that there is no danger of overstepping the bounds of normal physiologic action, however strong the specimen in hand. The use of so small a dose betrays us unfortunately from the Scylla of toxic action

to the Charybdis of uncertain reaction. It is a well known fact of physiology, that the stronger the stimulus the more nearly in accord are the results obtained on different individuals. This is particularly true of drug action. If $^{1}/_{16}$ of a grain of morphine be given to each of a series of persons, it will cause sleep in this person, nausea in that, wakefulness in a third, and perhaps a headache in a fourth. If, however, several grains are given to the same persons, it will cause narcosis in all. The same difference in reaction to small doses of medicine is seen in the effect of blood-pressure-raising drugs on different individuals. For this reason it is necessary to give first to the animals on which the tests are being carried out, a dose of a standard preparation, and then to determine how much of the preparation to be tested is required to bring about the same rise. The elimination of most drugs is so slow as to render this method valueless. With the exception of such drugs as amyl nitrite, which is eliminated within a few minutes, and adrenal principle, which is destroyed as rapidly, the effect of the first dose cannot, under the ordinary conditions of experiment, be allowed to pass off entirely before the next dose is administered, and there is for this reason a cumulative action, each dose adding to the effect of the previous one and rendering a true comparison impossible.

We thus come by a process of exclusion to the third method, the determination of the amount of a drug required to cause death. This amount is ordinarily determined by injecting into a series of animals progressively larger doses of the drug under consideration, and noting the smallest dose required to cause death. The method is therefore known as a minimal lethal (fatal) dose method. A large series of experiments show that by basing the dose on the weight of the animal, the activity of the preparation can be determined to within 10 per cent. That is to say, if a given dose is the smallest which will kill a given animal, $^{11}/_{10}$ of this amount will kill almost any individual of the same species, and $^{9}/_{10}$ of this amount will hardly ever kill. This fact bears out what has been said above concerning the agreement in the effects of large doses.

Granting then that the method gives concordant results, can we be at all sure that the toxic power which is estimated in this way is in accord with the therapeutic activity of the preparation? The

physiologic action of these drugs, on which their therapeutic value depends, is mainly a stimulation of the heart, shown by more forcible contraction of its wall. The drugs kill either by inducing a state of constant contraction (death in systole) or by overworking the heart muscle to such an extent that it gives way to a more or less sudden exhaustion with relaxation (death in diastole). In either case, the effect is primarily due to stimulation of the heart, and thus varies in accord with the physiologic or therapeutic activity. In this connection it may be as well to mention that occasionally in mammals, the respiration ceases before the heart has come to a standstill. This does not indicate any direct action of the drug on the respiratory centres, but is due to interference with the function of the medulla, dependent on the disturbance of its blood supply. The death is thus due to the stimulating action on the heart, however it may eventually occur. Granting then that the lethal dose method is not only exact, but also determines the physiologic activity, what animal is the best to use? It is often stated that as the drug acts on the medulla in mammals, as shown by respiration occasionally ceasing before the cardiac contractions, the drugs should be tested on frogs, in which it acts on the heart. As we have seen, the respiratory failure is really due to beginning cardiac exhaustion, and in reality there is no essential physiologic difference between the action of the drugs on the frog and on the guinea pig. The action of digitalis is largely exerted on the cardiac ganglia. In the frog these ganglia are in the heart, as may be demonstrated by the continuance of contractions after the removal of the organ from the body. In birds they are in the spinal cord, as is shown by the cardiac action continuing after the head is cut off. In mammals, however, the cardiac ganglia are in the base of the brain and any stimulus acting on these ganglia acts of course on the brain.

The frog is an unsatisfactory animal for the purpose of standardization, as its reaction to stimulation is markedly influenced by external surroundings, temperature, amount of moisture present in the cage, relation of time of injection to time of feeding, etc. The species of frog also makes a difference and, according to many authors, the time of year. Certain writers believe that season has of itself no influence, but that the differences found are dependent on different species being used, or on temperature. Al-

though the uncertainty arising from these factors may be avoided by great care, there will be a difference in different lots of frogs, and it is recommended by those who used the frog method, that a standard preparation of each drug be kept on hand and that each fresh batch of frogs be studied as to their relation to the standard before they are used for the purpose of testing new preparations. This makes the standard dependent on the keeping properties of a stock galenical, and these are exceedingly uncertain in many drugs. Any deterioration will result in a lowering of the standard for all subsequent preparations. For these reasons it seems wiser to use some animal which shows no such variation, is always of the same species, can be easily obtained, and is large enough to allow accurate and easy calculation and measurement of doses. The guinea pig fulfils all of these requirements, and has therefore been selected by us for use in our experiments. Moreover, as the guinea pig is very resistant to the action of alcohol, it is not necessary to evaporate alcoholic preparations to dryness before injecting them. The necessity for such evaporation when using frogs is of course well known.

It is a noteworthy fact, to which attention has often been directed, that the smaller animals require doses much larger in proportion to their weight. For instance, 0.75 c.c. tincture digitalis which can be given safely to a 250 gramme guinea pig, would correspond to 7.2 oz. to a 150 pound man, which would be far above a fatal dose. It has therefore been proposed that the dose should be based on the relative surfaces of the animals instead of on their weight. This would be the $\frac{2}{3}$ power of the weight, the square of the cube root. This would give a dose of little more than 1 oz. to a 150 pound man, which is about the largest dose which can be given safely. A series of experiments on guinea pigs of different weight have shown that this argument does not apply to them. Comparing pigs of about 225 grammes weight with others of 500 grammes, we find that upwards of twice as much is required to kill the larger animals. This shows that for animals of the same species the dose should be in proportion to the weight and not in proportion to the surface area.

In doing the routine work of standardization, the guinea pigs are first weighed, and then to one pig is given hypodermically the standard minimal lethal dose, to a second $^{9}/_{10}$ of this, and to a third $^{11}/_{10}$. If the drug is of proper strength, the two pigs

receiving the larger doses will die, while the third will recover. This being the case the drug or preparation may be passed as it is. If only the pig receiving $^{11}/_{10}$ dies, the preparation is to be concentrated 10 per cent. If all three pigs die, a fresh pig is given $^{8}/_{10}$ of the standard dose and the dose is reduced by tenths until a pig lives. The preparation is then diluted accordingly. If all three pigs live, a fresh pig is given $^{12}/_{10}$, and others increasing doses until two die. The preparation is then concentrated to agree with the smallest amount received by a pig which is killed.

By this method it is possible to make preparations which are always within 10 per cent. of the same strength. The standards on which I have decided, after a large amount of work with preparations from different houses, are as follows:

DOSE BASED ON A 250 GRAMME GUINEA PIG, AND PROPORTIONED TO WEIGHT IF THE PIG USED DOES NOT WEIGH THIS.

Drug	Fluidextract	Tincture	Extract
Apocynum	0.075 c.c.	0.75 c.c.	
Convallaria	0.075 c.c.	0.75 c.c.	
Digitalis	0.1 c.c.	1.0 c.c.	0.025 Gm.
Squill	$\frac{1890}{0.25}$ c.c.	0.75 c.c.	
	$\frac{1900}{0.5}$ c.c.		
Strophanthus	0.0025 c.c.	0.025 c.c.	

The most interesting point in connection with this table is the peculiar difference in the activity of the three preparations of squill. The alcoholic extract is about twice as strong as the acetic, or a little more, and the tincture about three times as active as the alcoholic extract, in proportion to drug strength.

We now turn to the consideration of the *heart depressants*. There are only three vegetable drugs in the Pharmacopœia whose most important physiologic action is a direct depression of the cardiac activity,—these being aconite, gelsemium, and veratrum. Related to these in action is a group of drugs which exert their most marked action on the voluntary muscles, causing loss of tone in these, and killing by respiratory, rather than cardiac, failure. This group includes physostigma, lobelia, and conium. The drugs of the digitalis series, which kill by depression resulting from over-

stimulation, show a very sharp line between their therapeutic and toxic doses. A dose slightly less than that which is required to cause death causes only slight toxic phenomena. With the drugs of this class, on the contrary, the toxic symptoms are manifested even under the influence of comparatively small doses and these increase gradually until death is reached. For this reason, the dosage of these drugs is not as sharply defined as that of the drugs previously considered, and it is necessary, in making a standard for these drugs, to arbitrarily fix a period of time within which the animal must die, if the drug is to be considered up to standard. This period has been fixed as three hours, as we have found that ordinarily a dose which will eventually prove fatal will do so within this time.

The *heart depressants* differ from the drugs of the digitalis series in another respect, each of them producing evident effects when given in sublethal doses. Aconite causes in many cases nausea, which is shown in the guinea pig by violent retching. As far as our observations are concerned, this animal never vomits. The irritant effect is also shown by the tendency of this drug to cause diarrhœa.

Gelsemium is likely to cause convulsions and these are frequently followed by paralysis, even in cases in which the animal eventually recovers. The guinea pig poisoned with gelsemium lies on the side, moving the legs feebly from time to time and breathing irregularly, and frequently only at long intervals. This paralysis may not come on until an hour or so after the administration of the drug, and in this case, recovery is likely to take place. If the paralysis occurs within twenty minutes of the time the drug is administered, the dose will generally prove fatal.

Veratrum stands between aconite and gelsemium in regard to these phenomena, causing convulsions less frequently than the latter, but being very likely to cause paralysis. Retching and diarrhœa, although not so common as with aconite, are frequently seen. It might be mentioned in this connection that, of the drugs spoken of in the previous article, apocynum frequently causes paralysis, even in animals which eventually recover, and squill and convallaria often cause convulsions. Digitalis is much freer from these sublethal toxic phenomena.

The drugs which have been mentioned as causing death by failure of the respiration can all be standardized by chemical means,

as their activity is largely dependent upon their alkaloidal content. Although aconite, gelsemium and veratrum contain alkaloids upon which their activity depends, their physiologic strength does not necessarily nor invariably vary in accordance with their alkaloidal content. The physiologic activity of aconite is mainly due to the aconitine which it contains, but this alkaloid contains in chemical combination a methyl and a benzoyl group, either of which may be split off during the handling of the drug and the loss of which renders the aconitine inactive, while still permitting it to respond to the chemical reactions of an alkaloid. This is particularly prone to occur on long standing of its preparations. Veratrum contains, in addition to veratrine, a series of alkaloids, among which may be mentioned protoveratrine, veratroidine and protoveratridine, which are almost entirely inactive, but which cannot be easily distinguished chemically from the active alkaloids. Gelsemium contains two alkaloids, gelsemine and gelseminine, the former of which has practically no effect on mammals but cannot well be distinguished by any chemical assay process. On account of the possibility, therefore, of obtaining misleading results from chemical assay alone, we are reduced to the necessity of substantiating such assays by physiologic means. Conium, physostigma, and lobelia all contain alkaloids upon which their pharmacologic and therapeutic activity depends, and the amount of which gives a direct indication of the therapeutic activity of the product. It is therefore not considered necessary to standardize these products physiologically.

After a large number of experiments extending over several months, the following standards have been adopted for the three drugs first mentioned. In each case the amount mentioned is injected subcutaneously into a guinea pig, and other pigs are given respectively $^{9}/_{10}$ and $^{11}/_{10}$ of the standard dose. If all three of these doses prove fatal, a smaller dose is given to a fresh pig; if none prove fatal, a larger dose is given to a fresh pig. If the dose given in the table proves fatal within three hours, and the pig receiving $^{9}/_{10}$ of this lives longer than this period, the drug is considered to be of standard quality. The doses given in the table are based on 250 gramme pigs and in case the pig weighs more or less than this amount, are made proportionate to its weight. The dosage is given in grammes of the drug and extract and in cubic centimetres of the liquid preparations.

Preparation	Drug	Fluidextract	Tincture	Extract
Aconite root	0.0100	0.0100	0.100	0.002
Aconite leaf	0.0150	0.0150	0.150	0.00375
Gelsemium	0.25	0.375	2.5	0.100
Veratrum	0.05	0.05	0.5	0.015

Feeling that perhaps the standard lethal doses of the drugs referred to in this paper might be more clearly understood if they were stated in a manner similar to that in use in describing the strength of bacterial toxins,—that is, by stating the number of units contained in a cubic centimetre of a standard preparation, we suggest the following system, namely, that the unit in this case be the amount required to kill one gramme of animal (guinea pig). By this method of calculation we have prepared the following table:

Preparation	Drug	Fluidextract	Tincture	Extract
Aconite root	25,000	25,000	2,500	125,000
Aconite leaf	16,600	16,600	1,660	66,000
Apocynum	3,300	3,300	330	
Convallaria	3,300	3,300	330	
Digitalis	2,500	2,500	250	10,000
Gelsemium	1,000	660	100	2,500
Squill		$\frac{1890}{1000}$ $\frac{1900}{500}$	330	
Strophanthus	100,000	100,000	10,000	
Veratrum	5,000	5,000	500	16,600

Of the drugs tabulated in the preceding portion of this communication only the following are sufficiently accurately provided with *chemical assay processes* to enable us to make comparisons: digitalis; aconite root; aconite leaf; gelsemium; veratrum.

Digitalis.—Attention is first called to the article by Reed and Vanderkleed on the standardization of digitalis preparations, published in the March, 1908, number of the AMERICAN JOURNAL OF PHARMACY. There, on page 119, is given a table showing the relationship between chemical assay for digitoxin and physiologic assay based upon lethal dose for guinea pigs, for nine preparations. During the past year, the results as shown in the following table indicate that the minimum lethal doses as obtained by Dr. Reed two years ago were slightly smaller than those obtained by Dr. Githens during the past year, when compared with the results

obtained by chemical assay as described in the article mentioned above.

No.	Preparation	Chem. Assay Gramme Digitoxin in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Per cent. Digitoxin Calculated from a Lethal Dose of 1 c.c. of Tinct.
1	Tinct. U.S.P.	0.0326	0.8 c.c.	0.02608
2	Tinct. U.S.P.	0.0329	0.8 c.c.	0.02630
3	Tinct. U.S.P.	0.0290	1.0 c.c.	0.02900
4	Tinct. U.S.P.	0.0280	1.1 c.c.	0.03080
5	Tinct. U.S.P.	0.0380	0.9 c.c.	0.03420
6	Tinct. Fat free	0.0410	0.9 c.c.	0.03690
7	Tinct. Fat free	0.0328	1.1 c.c.	0.03690
8	Tinct. Fat free	0.0375	0.9 c.c.	0.03375
9	Tinct. Fat free	0.0440	0.75 c.c.	0.03300
10	Tinct. Fat free	0.0240	1.25 c.c.	0.03000
11	Tinct. Fat free	0.0365	0.8 c.c.	0.02920
12	Tinct. Fat free	0.0290	1.0 c.c.	0.02900
13	Powdered Ext.	0.763 per cent.	0.031 Gm.	0.02370
	Average			0.03061

A study of the table of March, 1908, shows that an assay of about 0.025 Gm. digitoxin per 100 c.c. corresponded closely with a lethal dosage for 240 Gm. guinea pigs of about 1 c.c. A careful scrutiny of the above results shows not quite so uniform an agreement, but, on the whole, a minimum lethal dose of 1 c.c. corresponds fairly closely with an assay of 0.030 Gm. digitoxin per 100 c.c. The third column, consisting of figures representing the products obtained by multiplying together the figures in columns 1 and 2, shows how nearly concordant the results obtained ran, and corresponds to percentage of digitoxin *calculated from* a lethal dosage of 1 c.c. of tincture, 0.1 c.c. of fluidextract, or 0.025 Gm. powdered extract. The average of this column is 0.0306. Continued work on this interesting assay has shown that the purity of the crystalline digitoxin obtained depends largely on the manipulation of the bulky lead subacetate and sodium phosphate precipitates (see AMER. JOUR. PH., 1908, p. 118). A centrifuge is now being installed in our laboratory suitable for sedimenting these preparations,—and by its use, it is hoped that a higher degree of purity of the separated digitoxin will be obtained, insuring results still more nearly concordant with physiologic assay.

Aconite Root and Leaf.—The chemical assay methods employed for all aconite preparations in the following table were essentially those of the U.S.P.

No.	Preparation	Chem. Assay Gramme Aconitine in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Per cent. Aconitine calc. from a Lethal Dose of 0.1 c.c. of Tincture
1	Tinct. U.S.P.	0.0411	0.130 c.c.	0.053
2	Tinct. U.S.P.	0.0614	0.075 c.c.	0.046
3	Tinct. U.S.P.	0.0480	0.100 c.c.	0.048
4	Tinct. U.S.P.	0.0425	0.125 c.c.	0.053
5	F. E. (leaf)	0.2400	0.020 c.c.	0.048
6	F. E. (root)	0.4400	0.0075 c.c.	0.033
7	F. E. (root)	0.4150	0.0075 c.c.	0.031
	Average			0.044

A survey of the above table shows far less concordance between chemical assay and lethal dose than in the case of digitalis. The agreement is fairly close in the case of the tinctures and of the fluidextract of leaf, but the two fluidextracts of root possess a degree of toxicity about 25 per cent. greater than should have been expected from the chemical assay. A continuation of the collection of data will throw additional light on this peculiar observation.

Gelsemium.—A comparison of the results of chemical assay for total alkaloids in gelsemium with its minimum lethal dose was first undertaken at the suggestion of Prof. L. E. Sayre, who describes the results first obtained on page 855 of the 1908 Proceedings of the American Pharmaceutical Association. Attention is also directed to the reported discussion on Prof. Sayre's paper on pages 851–8 of this volume. The following table shows the results obtained since that time,—the chemical assay method used being that of Webster as described by Sayre in the article mentioned above:

No.	Preparation	Chem. Assay Gramme Alkaloid in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Per cent. Alkaloids calc. from a Lethal Dose of 0.375 c.c. of Fluidextract
1	Tincture	0.0316	2.00 c.c.	0.17
2	Tincture	0.0715	1.25 c.c.	0.23
3	Tincture	0.0538	2.00 c.c.	0.29
4	Fluidextract	0.400	0.375 c.c.	0.40
5	Fluidextract	0.400	0.375 c.c.	0.40
6	Fluidextract	0.400	0.375 c.c.	0.40
7	Fluidextract	0.500	0.300 c.c.	0.40
8	Fluidextract	0.550	0.3 c.c.	0.44
9	Fluidextract	0.465	0.4 c.c.	0.50
10	Solid extract	2.185 per cent.	0.09 Gm.	0.52
	Average			0.375
	Average on fluid and solid extracts alone			0.437

This table serves to demonstrate the necessity for physiologic control of the chemical assay for gelsemium and the worthlessness of the latter unless accompanied and checked by the physiologic test. Just contrary to the results obtained with aconite, the *tinctures* of gelsemium are much more toxic than the fluidextracts, on the basis of equivalent amounts of total alkaloid. This is probably due to a higher proportion of highly active gelseminine being taken up by the prolonged percolation which occurs in the preparation of the tincture.

Veratrum.—The chemical results, expressing total alkaloids, in the following table were obtained by the following method:

The fluidextract, 10 c.c., or the tincture, 100 c.c., is evaporated on purified oak sawdust, and the dried mixture macerated with a mixture of ether, 80 c.c., chloroform, 20 c.c., and ammonia water, 10 per cent.—10 c.c. An aliquot part of the ethereal extract is shaken out with 5 per cent. acetic acid, rendered alkaline with ammonia, shaken out with chloroform, evaporated, dried, and weighed.

In the case of the solid extract, 2 or 3 grammes are dissolved in 50 per cent. alcohol, filtered onto purified oak sawdust, and finished like the fluidextract and tincture.

No.	Preparation	Chem. Assay Gramme Alkaloid in 100 c.c.	Phys. Assay, Min. Lethal Dose for 250 Gm. Pigs	Per cent. Alkaloids calc. from a Lethal Dose of 0.5 c.c. of Tincture
1	Tincture	0.1	0.5 c.c.	0.100
2	Tincture	0.102	0.5 c.c.	0.102
3	Tincture	0.078	0.75 c.c.	0.117
4	Solid extract	4.0 per cent.	0.015 Gm.	0.120
5	Fluidextract	1.0	0.05 c.c.	0.100
6	Fluidextract	1.145	0.065 c.c.	0.149
	Average			0.115

Except for No. 6 in the above table, the lethal dose of which is abnormally high in comparison with the chemical assay, the activity of preparations of veratrum seems to agree quite closely with the percentage of total alkaloids. The chemical assay of veratrum appears therefore to possess undoubted value.

It is the intention of the authors to continue the tabulation of comparative results of physiologic and chemical assay of these drugs, as well as to start similar series of comparisons on conium, physostigma, and lobelia.

RESEARCH LABORATORIES OF
H. K. MULFORD COMPANY.

A CONTRIBUTION TO THE HISTORY OF "PINK-ROOT."*

By M. I. Wilbert.

Spigelia marilandica illustrates, as well perhaps as any drug now used, the interesting comedy of errors that may be developed by following up the history of the origin and uses of a drug that has passed through the vagaries incident to its empiric use in medicine.

Much of the confusion concerning this particular drug, and its adulterant, has been unravelled by W. W. Stockberger in his comprehensive and scholarly monograph on "Pink-root and its Substitutes," published in part as Bulletin 100 of the Bureau of Plant Industry and in full in the *Pharmaceutical Review* for 1907, also as a separate by the Pharmaceutical Review Publishing Co., Milwaukee, 1907.

Stockberger, however, leaves two rather interesting questions unanswered, at least directly: (1) Who was the first to recognize the then common adulterant of spigelia as *Phlox carolina?* (2) What was the nature of the second "pink-root" frequently referred to as having been in use in this country during the earlier decades of the nineteenth century?

I believe that the direct answer to the first question is to be found in one of the very few references that Stockberger appears to have overlooked in the compiling of his admittedly comprehensive bibliography of the literature on "pink-root."

The first edition of the National Dispensatory (1879) in the monograph on spigelia, evidently written by Maisch, says: "Spigelia is sometimes met with as an admixture of serpentaria, and is not infrequently found mixed with some few roots of several plants, doubtless from careless collection. A few years ago a very different root was seen in the market, which Dr. A. W. Miller (1875) ascertained to have been derived from *Phlox carolina*, Lin., which plant is known in some parts as Carolina pink. This root is lighter in color, the rootlets are straight or but slightly curved, and their cortical portion is easily removed, exposing a straw colored ligneous thread."

* Presented at the Historical Section, A. Ph. A., 1909.

The first announcement of this adulterant appears to have been made at a pharmaceutical meeting of the Philadelphia College of Pharmacy, February 16, 1875, when "Dr. Miller presented a sophistication of spigelia, to which his attention was drawn by S. W. Brown of Manayunk. Upon inquiry he learned it was known in the market as East Tennessee pink-root; but the plant from which it is derived has not been ascertained. It is said to be largely sold to manufacturers of fluidextracts."

At the annual meeting of the American Pharmaceutical Association, in Boston, in 1875, Dr. A. W. Miller, as chairman of the committee on adulterations and sophistications, presented the final report, quoted by Stockberger, in which he gives a more detailed account of the adulterated pink-root and records securing an additional supply of this "so-called East Tennessee pink-root" from a commission merchant in Philadelphia.

Miller also reports addressing a letter of inquiry to Messrs. Wallace Bros., of Statesville, North Carolina, who "have since been able to identify the sample as the root of *Phlox carolina* known with them as the Carolina pink."

From the available publications it would appear that the adulteration was brought to the attention of Dr. A. W. Miller by S. W. Brown, of Manayunk, and that Dr. Miller submitted samples of the root to Wallace Bros., who identified the same as *Phlox carolina*.

It is quite likely that the claim recorded by Stockberger as having been made by M. E. Hyams is correct, as a personal letter recently received from Dr. A. W. Miller recalls that a Prof. Hyams was formerly in the employ of Wallace Bros. or affiliated with them as botanist, and it is quite probable that the inquiry from Philadelphia was submitted to him so that the sequence would be complete and Prof. M. E. Hyams really the first to mistake, as True and others have pointed out, Ruellia as Phlox.

An even more interesting question is the one as to the identity of the second pink-root used in Eclectic and to some extent also in domestic practice during the earlier decades of the nineteenth century.

Dr. Benjamin Smith Barton, in his "Collections for an Essay Towards a Materia Medica of the United States," says: "The *Silene virginica* or ground pink, as it is called in some parts of our country, is another native anthelmintic. A decoction of the root

is used and is said to have been found a very efficacious remedy." In a footnote Barton says: "From the information of my friend, the late Dr. James Greenway, of Virginia."

Dr. John Redman Coxe in the early editions of the American Dispensatory says: "*Silene virginica,* ground pink. This species of silene or catchfly is abundant in many parts of the United States. Some of the Indians say it is a poisonous plant. In decoction the root has been found to be an efficacious anthelmintic."

Many other early writers on American materia medica mention this particular member of the pink family which appears to have met with some use both at home and abroad and may, in part at least, account for the practice observed by Flückiger and Hanbury who note that spigelia or pink-root is sometimes erroneously latinized in price lists as "*Radix Caryophylli.*"

In some of the early Eclectic works on materia medica, *Silene virginica* was recommended as a vermifuge and a nervine. It was popularly known as "wild pink, pink catchfly, fire pink, ground pink, and Virginia pink." No reference to the use of this root could be found in recent literature and an inquiry addressed to some of the larger herb dealers in the country failed to find a single one who had any knowledge of the drug or its uses, and practically the only available reference to it, of recent date, is the continuation of a rather misleading notice in the United States Dispensatory.

The earlier editions of the United States Dispensatory say: *Silene virginica,* catchfly, wild pink, an indigenous perennial plant growing in Western Virginia and Carolina, and in the States beyond the Alleghany Mountains. Dr. Barton in his "Collections" states that a decoction of the roots is said to be efficacious as an anthelmintic. We are told that it is considered poisonous by some of the Indians. The *S. pennsylvanica* which grows in the eastern section of the Union from New York to Virginia probably possesses similar properties.

The 19th edition of the United States Dispensatory (1907) says: Silene—*Silene virginica* L. (Fam. Caryophyllaceæ), catchfly, wild pink. The wild pink of West Virginia and the Carolinas was considered by the Indians poisonous and by Barton an anthelmintic.

The latter description is short, positive, and pithy, and is evidently the product of shears and blue pencil, but would it not be more in keeping with a book of reference to delete it entirely or to reconstruct it and allow it to appear as a memorial of a one

time popular remedy, that as Hollembaek and others assert, was frequently employed as a substitute for the *Spigelia marilandica?*

And this suggests that ponderous tomes like the United States Dispensatory frequently contain much that is interesting and amusing, if recognized, and sadly misleading if one unwittingly relies on them for the information that they are expected to contain. Reverting for a moment to spigelia, it will be worth while to read Stockberger's monograph on this drug and then to peruse the peculiar conglomerate of old and new that is presented in the United States Dispensatory as a description for the same.

Among the interesting pieces of information still offered that had their origin before the Civil War, probably before the introduction of railways, is the reference to the emigration of the poor Indian and the marketing of spigelia in huge casks or bales, from St. Louis by way of New Orleans, and the added piece of information that "That contained in casks is to be preferred, as less liable to be damp and mouldy."

Another interesting bit of information is the assertion that: "It is frequently necessary to separate the spigelia from the various adulterant roots. Among the most important of these may be mentioned the roots of certain small vines which frequently twine around the spigelia stem; these roots can be distinguished by their being long, slender, crooked, yellowish, thickly set with short capillary fibres, and much smaller and lighter colored than is pink-root."

This statement is evidently taken from a book by James Ewell, physician in Washington, formerly of Savannah, who early in the nineteenth century expressed the belief that the deleterious effect of commercial spigelia was due to the root of this particular vine.

John Redman Coxe, in the 9th edition of the American Dispensatory, refers to this statement made by Ewell and quotes a letter from a Mr. Porcher, who controverts the theory and quotes a Mr. Stephen Elliot as being of the opinion that the poisonous property observed is characteristic of spigelia itself.

It would appear desirable that, granting that "commentaries" are to be simple compilations, they be so labelled and that wherever possible the original reference or the approximate date be appended so as to give at least some indication of the reliability of the information offered.

THE HISTOLOGY OF THE RHIZOME AND ROOTS OF PHLOX OVATA L. (PHLOX CAROLINA L.).*

By Henry Kraemer.

For some time I have felt the importance of making studies of the structure of the underground portions of American plants, as there are so many vegetable fragments of unknown origin in many cases which are found admixed with the more common drugs, and which have a superficial resemblance to them. Thus, unless careful garbling is practised, these foreign plant parts may not only be found as an admixture, but as an entire substitute for the genuine drug.

My interest in *Phlox carolina* dates back some twelve years when, at my request, Mr. C. D. Beadle, of the Biltmore Herbarium, sent me a number of plants which he collected in the mountains of North Carolina. While I did not make an extended study of the material at the time, I examined it sufficiently to lead to the conclusion [1] that the material which Greenish described in his paper did not answer to the description of *Phlox carolina*. My main object at that time was to determine the origin of a substitute for Spigelia, in which one of my students at Northwestern University discovered by accident the presence of calcium carbonate. This substitute was shown subsequently and independently by Stockberger [2] and Holm [3] to be the rhizome of *Ruellia ciliosa*.

In connection with their studies on *Spigelia marilandica* and *Ruellia ciliosa*, these authors have also described the structure of *Phlox ovata* (*Phlox carolina*). While the papers of Stockberger and Holm are excellent contributions to the subject, there are still some features which should be brought out more distinctly, especially from the practical pharmacognostic point of view. Stockberger considers that the rhizome and roots of *Phlox ovata* "rarely or never occur as a substitute for Spigelia," and I agree with him in a measure, but its occurrence is still reported and, besides, workers do not seem to be clear in regard to the characters of the drug. I do not, however, agree with the statement made by Stockberger that "the root so generally described and studied as

* Read before the Scientific Section of the American Pharmaceutical Association, May, 1910.

Phlox must be referred to *Ruellia*," which latter drug I hope to take up later.

In order that errors may be eliminated from the literature, it should be pointed out that in the English translation of Solereder's "Systematic Anatomy of the Dicotyledons," which appeared as recently as 1908, the translators continue the mistake in the original German edition of accepting as true the description given by Greenish [4] of what he had reason to suppose was *Phlox carolina*, but which it has since been seen was not an authentic specimen. It should also be pointed out for the benefit of practical workers that the material studied by Professor Greenish was drug material, some of which was supplied by Professor Maisch, but neither of them is open to criticism, both of them having accepted as probably genuine what was supplied them, as was then more customary. Indeed, Professor Greenish did a very excellent piece of work, and nothing would have been left to be desired if he had known the name of the plant from which the material with which he worked was derived and had named his paper accordingly, that is, by substituting the name *Ruellia ciliosa* for *Phlox carolina*. Later experience also shows that it is extremely hazardous to base a study of a vegetable drug on the commercial material alone, and that no studies of this kind can be considered entirely reliable or authoritative which are not based upon material collected from or compared with that derived from plants which have been identified.

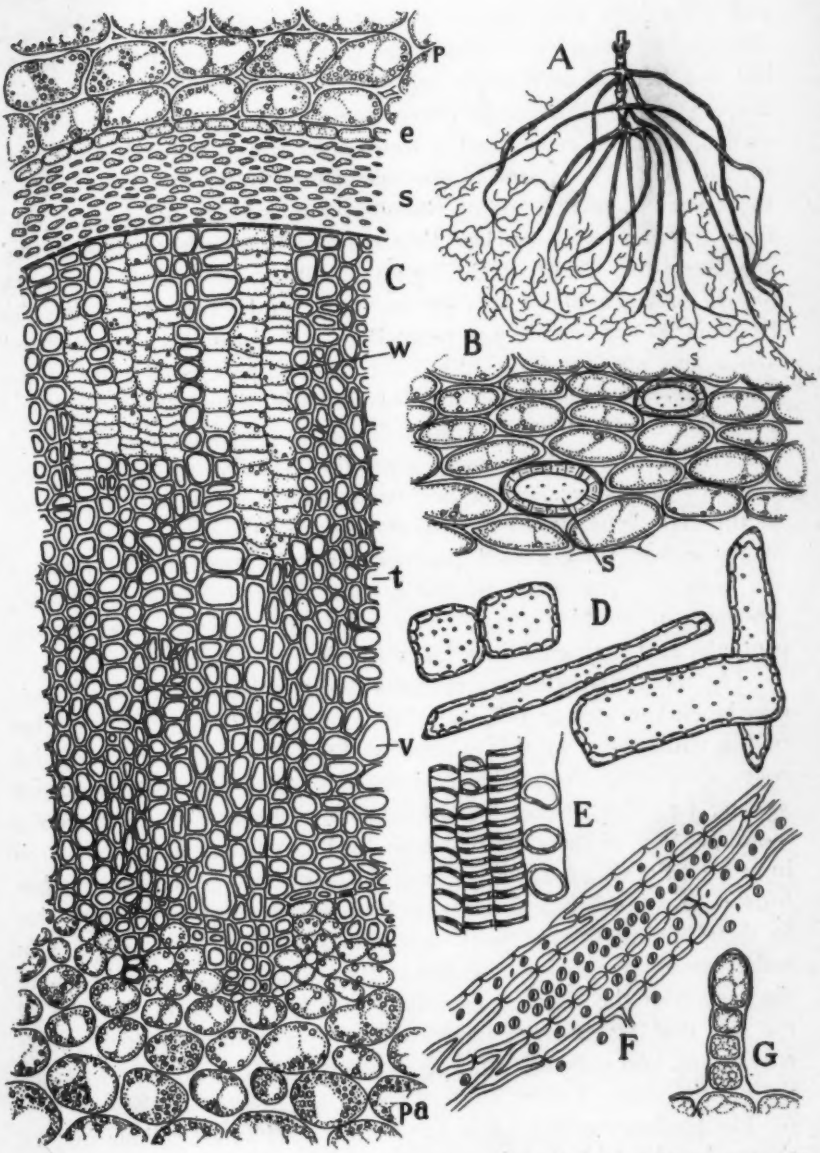
The species belonging to the genus *Phlox* are found chiefly in North America, where they number about thirty. The plants are mostly herbaceous perennials, a number of the species being extensively cultivated for ornamental purposes. The stems are either decumbent or ascending, or in some cases they are slightly decumbent near the base and then ascending, as in *Phlox ovata*. *Phlox ovata* is found in open mountainous woods from Alabama to Pennsylvania, and there are some colored plates representing this plant in the *Botanical Magazine* (t. 528 and 1344). According to Gray, in his "Flora of North America," *Phlox carolina* is merely a taller form of *Phlox ovata*, but having narrower, more tapering leaves and pointed calyx teeth, approaching *Phlox glaberrima*. According to botanists to-day, the form with ovate or ovate-lanceolate leaves is regarded as the typical species, and the name *Phlox carolina* has been superseded by *Phlox ovata*.

Phlox ovata generally attains a height of from 3 to 6 decimetres,

The stems are cylindrical, smooth, and the diameter is from 2½ to 3½ mm. Thus, they are seen to be slender stems, and in order to maintain their perpendicular position would need to be quite woody, especially in the lower portion, which they are. The so-called rhizome, which is merely an extension of the over-ground stem, is usually vertical, comprising from two to four nodes, and usually 1 to 2 cm. long. From the nodes arise from two to four comparatively thick roots, which are sometimes nearly 2 mm. in diameter in the fresh state, from 1 to 2 decimetres long, unbranched, and produce a large number of fine rootlets, especially near the free ends (Fig. A). The commonly vertical character of the rhizome of *Phlox ovata* is one of the features which distinguishes it from the rhizomes of both Spigelia and Ruellia, although it should be stated that occasionally decumbent stems are found which produce roots at the nodes. In neither case is that part of the stem producing roots a true rhizome.

The rhizome, or underground part of the stem, is characterized by a strong development of woody tissue, which in transverse section occupies about one-half of the radius. The bark is about 0.5 mm. in diameter, the xylem and phloem together are about 0.9 mm. in diameter, and the radius of the pith is 0.3 mm.

Histological Characters of Rhizome.—The epidermis in transverse section is made up of rounded tabular cells and is surrounded by a cuticle which is more or less lignified and 8 to 10 microns in thickness. Beneath the epidermis are two to four rows of collenchymatous cells, the remainder of the cortex being made up of about twelve rows of parenchyma cells, the walls of which are about 5 microns thick, the cells themselves being from 40 to 80 microns in diameter. All of the cells of the cortex are rich in protoplasmic contents, and sometimes contain a considerable number of small starch grains, 1 to 3 microns in diameter. Beneath the cells of the cortex there is usually a well-defined ring of endodermal cells, which may be more or less lignified, and which may also contain a few small starch grains. Beneath the endodermis is a layer of pericambial cells, which show one or two tangential divisions. Next beneath is the sieve, which is made up either of thin-walled, somewhat tabular cells, or of oval, very thick-walled cells. The sieve cells are rich in protoplasmic contents, and frequently contain a number of starch grains. The xylem portion of the fibrovascular bundles (Fig. C) is made up of at least two,



Phlox ovata L. (*Phlox carolina* L.): A, lower portion of plant showing long roots with numerous rootlets at the ends; B, parenchyma from cortex of rhizome showing two sclerotic cells (s); C, cross-section of portion of rhizome showing parenchyma of cortex (p) which contains protoplasm and starch grains, endodermis (e), leptome (s), tracheæ (v), libriform (t), wood parenchyma (w), parenchyma of pith containing starch grains and protoplasm (Pa); D, isolated sclerotic cells from cortex; E, vessels with annular and spiral thickenings; F, libriform cells; G, glandular hair from the leaf.

and frequently three areas—an outer layer composed of compact, strongly lignified cells, which are present in more lignified stems but not here illustrated; a middle layer, as in Fig. B, in which there are radial rows of parenchyma cells separating the thick-walled, lignified cells; and a continuous zone of lignified cells, as in Fig. C. The tracheæ are marked with bordered pores, and those near the centre of the rhizome have annular and spiral markings, the number of tracheæ thus marked being rather striking and characteristic. Most of the lignified cells of the xylem are in the nature of tracheids, which are narrower and longer than those in Spigelia, being usually not more than 20 microns in diameter and about 500 microns long (Fig. F). The parenchyma cells in the outer layers of the wood not infrequently show the presence of a number of small starch grains similar to those already described. Underlying the xylem tissue somewhat tabular cells, resembling those of the sieve, sometimes occur, but for the most part all of the cells beneath the xylem, constituting the pith, are made up of somewhat thick-walled parenchyma cells resembling those of the cortex. The walls of these cells are non-lignified, and are wanting in simple pores. The cells are rich in protoplasmic contents, and may contain a large number of starch grains.

The most characteristic features of the rhizome of *Phlox ovata* may be enumerated as follows: (1) The upright or vertical position of the rhizome; (2) the few rather long and comparatively thick roots extending from the nodes; (3) the comparatively thick xylem; (4) the absence of an internal phloem, the fibrovascular bundles being of the collateral type, and (5) the presence of starch in at least the rhizomes of the fruiting plants. The fact that neither Stockberger nor Holm found starch in this rhizome is probably due to their having worked with material in which it was present in rather small quantities, the amount varying unquestionably with the season of the year. I especially mention this point, in view of the fact that Stockberger places Phlox in a group in which starch is wanting, and calls attention to its supposed absence as a differentiating character.

The tendency of this plant to produce mechanical cells is further shown by the fact that some of the cells of the pith as well as of the cortex are thick-walled, strongly lignified, the walls being marked by rather fine simple pores (Figs. B, D). These cells as they occur in the pith are either cubical, or elongated and with square ends, while those in the cortex are narrow, with

pointed or oblique ends, and from 100 to 300 microns in length. Somewhat similar stone cells are found in the stem of *Phlox pilosa* L. If the material containing these cells should be relatively abundant in a mixture, their presence would give another character for distinguishing the rhizome of Phlox from that of Spigelia. The stone cells in Ruellia are different in shape, and in addition are associated with cells containing calcium carbonate. The presence of these special, thick-walled lignified cells in the rhizome of Phlox may, however, be of infrequent occurrence, like the bast fibres in belladonna, which I have only occasionally seen, but which have been described by Schrenk, and therefore may not be of assistance in the identification of the drug. It might be mentioned in this connection, however, that groups of bast fibres have been found in *Phlox aristata* Michx., and a ring of bast fibres in the stem of *Phlox longifolia* Nutt., *P. Douglassi* Hook., and *P. acuminata* Pursh.

Histological Characters of Root.—A transverse section of the root shows (1) ordinary epidermal cells with root-hairs; (2) a hypodermis made up of radially elongated, more or less pentagonal cells; (3) a cortex, consisting of 12 to 20 rows of ellipsoidal rather thin-walled parenchymatous cells, which are rich in protoplasm and may contain small starch grains; (4) a peripheral layer of the central cylinder; (5) endodermis; (6) internal layer of cortex, and (7) within this there is in the very young roots a triarch to pentarch radial fibrovascular bundle, which later becomes collateral and closely resembles in structure that of the rhizome.

While the stem is free from hairs the leaves have rather striking glandular hairs (Fig. G), which are found on the principal veins near the base of the leaf. The histological characters of the leaf have been very well given by Holm, and it therefore does not seem necessary to consider them here.

I may say in conclusion that I am engaged in the study of the structure of the underground parts of other species of Phlox, as possibly the rhizomes and roots of other species may occur as admixtures in drugs, and besides the genus is of great interest botanically.

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[3] Am. Jour. Pharm., **78**, p. 553; **79**, p. 51 (1907).
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OIL OF SESAMUM—ITS USE IN PHARMACY.*

By Otto Raubenheimer, Ph.G., Brooklyn, N. Y.

Oleum sesami, sesame oil, benne oil, gingelli oil, gingelly oil, or teel oil is the fixed oil expressed from the seeds of *Sesamum indicum* L. (Fam. Pedaliaceæ). The sesame plant is indigenous to India, but is largely cultivated also in China, Japan, and most Oriental and tropical countries. According to Miss Alice Henkel, assistant in drug plant investigations, Bureau of Plant Industry, U. S. Department of Agriculture, sesame has also been cultivated to some extent in the Southern States and is said to run wild in the extreme south. The yield of oil is from 47 to 57 per cent. It has a pale yellow color, is nearly inodorous, and has a bland nut-like pleasant taste.

Table of constants: Specific gravity at 15° C., 0.920–0.924; specific gravity at 98° C., 0.867–0.870; solidifying test, 4° C.; iodine value, 103–112; and saponification value, 189–193.

Optical rotation, slightly dextrogyrate, + 1 to + 9. The latter is due to sesamin $C_{18}H_{18}O_5$ and phytosterol. Sesame oil consists essentially of the glycerides of oleic and linoleic acids, with small proportions of stearin, palmitin, and myristin. The two principal advantages of oil of sesamum are that it is a non-drying, or rather a semi-drying oil and that it does not readily turn rancid. The best qualities are largely used in the manufacture of oleomargarine.

OLEUM SESAMI SUPERIOR TO COTTONSEED AND OLIVE OILS.

It is official in most of the foreign pharmacopœias and has been admitted to the recently published pharmacopœias, replacing olive oil in a great many galenical preparations. As it is recognized by the Eragaenzungsbuch (supplement to the German Pharmacopœia), it will undoubtedly become official in the new (5th) edition of the Arzneibuch.

The colonial addentum of the British Pharmacopœia permits the use of sesame oil in India, the African, Eastern, and North American colonies, in the preparation of the official liniments, oint-

*Read and demonstrated with specimens before the meeting of the N. Y. State Pharmaceutical Association, June 21, 1910, at Saratoga Springs.

ments, and plasters for which the British Pharmacopœia orders that olive oil should be used.

Sesame oil has the following advantages over cottonseed and olive oil:

1. It does not readily turn rancid.
2. It is easily saponified even by cold process.
3. It is a semi-drying oil.
4. It is not gummy and sticky.
5. It is more readily absorbed by the skin.
6. It is thinner than cottonseed oil although of the same specific gravity, in other words it possesses less viscosity.
7. It does not congeal until —5° C. and solid particles do not separate until —3° C., while cottonseed oil congeals at 0° C. and solid particles separate already at +12° C., and olive oil congeals at 0° C. and solid particles do not separate at +10° C. For the latter reason sesame oil is much to be preferred in colder climates.
8. Its price is reasonable, $1.00 or less per gallon according to quantities.
9. Its price is not apt to market fluctuation as, owing to the *extensive cultivation*, the *rapid growth* of the plant, and the *double annual harvest* of the seed, a very large quantity of sesame oil is produced.

OLEUM SESAMI DELETED FROM THE U.S.P. VIII.

The leaves of sesame were official in the U.S.P. 1830 (1st revis.) to U.S.P. 1880 (6th revis.) inclusive. Sesame oil was official in the U.S.P. 1830 to U.S.P. 1890 (7th revis.) inclusive. Unfortunately, however, it was not admitted again into the U.S.P. VIII. I am informed by a member of the former Revision Committee that the step was taken because the general opinion of the majority of the members was that sesame oil was antiquated and was no longer in use.

Those interested in pharmaceutical history, and I hope their number is on the increase, will undoubtedly be pleased to hear that oleum sesami is a very old if not *the oldest* oil known. Herodotus (born 484 B. C.), the father of history, states that it was the best known oil at that time. According to G. P. Forrester in the *Chemist and Druggist*, London (abstracted in the *American Druggist*, June 13, 1910, p. 308), the word sesame occurs in an Egyptian document of about 1500 B. C.

Any of you further interested in the history of sesamum I would recommend to look up the masterwork of the German pharmaceutical historian, Dr. Hermann Schelenz, "Geschichte der Pharmazie."

OLEUM SESAMI SHOULD BE ADMITTED INTO THE U.S.P. IX.

I can, however, not agree with the decision of the old Revision Committee that sesame oil is antiquated and no longer in use. It has been official right along in a number of pharmacopœias, it has been used officially and unofficially in the preparations of a large number of galenicals and it has been admitted to all the recent pharmacopœias. As I said before the British Pharmacopœia sanctions the use of oil of sesamum in place of olive oil in the British Colonies. Inasmuch as the revisers of the foreign pharmacopœias are convinced of the value of this oil and in view of the many experiments, for a period of several years, which I and other pharmacists have made with oil of sesamum in various galenical preparations, I sincerely hope that the present Revision Committee will consider the admission of this oil into the new U.S.P. and its use in several galenicals.

EXPERIMENTS WITH OLEUM SESAMI.

The use of sesame oil by the writer dates back about 20 years, when he prepared a hair oil or macassar oil, colored red with alkanet and suitably perfumed, which in those days had a very large sale, undoubtedly due to the fact that it was less oily, less sticky and gummy, and more readily absorbed and penetrating than others. Oil of sesamum has been used for anointing in ancient times and is mentioned as such in the Bible and is described for this and other uses by Dioscorides, that most important author, whose works on pharmacology and the entire materia medica were authoritative down to the sixteenth century. Xenophon, the last of the three great Greek historians, writes in his Anabasis or Expeditio Cyri (371 B.C.), an account of "the retreat of the ten thousand," a part of the army of Cyrus, after the unfortunate battle of Kunara, that by the application of sesame oil they prevented their hands and feet from becoming frostbitten.

The following are a few of the external preparations with

which I have experimented for a number of years. Specimens are herewith submitted and some of the galenicals will be prepared before you extemporaneously.

LINIMENTUM AMMONIÆ.

Undoubtedly all of you are familiar with the shortcomings of the present U.S.P. formula for this liniment, which are: 1. Four ingredients instead of two. 2. The cumbersome method. 3. The yellow color. 4. The separation into layers. 5. The thinness when freshly prepared. 6. The thickening by age.

It is certainly impracticable to mix four ingredients together when five cents' worth of hartshorn liniment is called for, the U.S.P. stating: "The liniment should be freshly prepared when wanted."

Although Eugene Dieterich, the great German manufacturing pharmacist, is generally credited with the original use of sesame oil in the preparation of ammonia liniment, I have found that as early as 1884, F. M. Alcock states on page 282 of the *Pharmaceutical Journal and Transactions,* London: "Sesame oil makes a more satisfactory ammonia liniment than olive or other oils;—even after standing three (3) months there is no sign of separation and the liniment presents a beautiful creamy consistency and color but slightly altered during the time stated."

From experiments during a period of several years I have arrived at the conclusion that as per demonstration you can prepare an ideal ammonia liniment by shaking together: sesame oil, 3 parts by weight, and ammonia water, 1 part by weight.

My opinion is that it is an advantage, being easier and cleaner, to weigh the ingredients instead of measuring them.

This liniment has the following advantages:

1. It contains only 2 ingredients.
2. It can be prepared quickly and easily.
3. The resulting liniment is snow-white.
4. It is homogeneous and does not separate into two layers.
5. It has the proper creamy consistency, not too thick and not too thin.
6. It is permanent and will not thicken materially by age, as you can convince yourself by a specimen over a year old.

LINIMENTUM CALCIS.

Although the U.S.P. formula for lime liniment or carron oil, *i.e.*, equal volumes of linseed oil and lime water, is perfectly satisfactory, I wish to call your attention to the liniment prepared with oleum sesami which is official in the Japanese Pharmacopœia III, 1905. As you see by this extemporaneous preparation equal parts, by weight, of sesame oil and lime water will give at once a beautiful, white, homogeneous liniment.

LINIMENTUM CAMPHORÆ.

The employment of heat in the present U.S.P. directions has unquestionably been the direct cause of court decisions that the preparation *cannot* contain 20 per cent. of camphor.

Sesame oil is much to be preferred to cottonseed oil: first, because it is not gummy or sticky; second, because it is readily absorbed by the skin; and third, because it is a better solvent for camphor as the same dissolves easily without the aid of heat.

Circulatory displacement, without heat, in my experience is *the* ideal method of preparing a full-strength camphorated oil, which synonym will undoubtedly be admitted in the next revision.

Our U.S.P. should include besides a short physical description including specific gravity also an assay for determining the strength of camphor liniment. The Austrian Pharmacopœia VIII, 1906, which orders one part of camphor and three parts of oleum sesami, gives the following approximate method for determining the strength: When 10 c.c. of oleum camphoratum and alcohol are well shaken together in a graduated tube, then the separated alcoholic layer should not measure less than 13 c.c. While this is not an exact assay, it will certainly serve as an approximate test which can be easily applied by the average pharmacist. Experiments in the application of this test to the U.S.P. camphor liniment are going on in my laboratory and will be published in due time.

INFUSED OILS.

Infused oils and quite especially *Oleum Hyoscyami Infusum* N.F. or, as it is named by the foreign pharmacopœias, "coctum." The process employed in the N.F., as well as the foreign pharmacopœias, is the Eugene Dieterich method, consisting of macerating

the ground drug with ammoniated alcohol to liberate the alkaloids and then infusing with the oil. Olive oil was formerly used, but sesame oil has replaced it in the newer pharmacopœias and sesame oil should most certainly displace the poor mixture of lard and cottonseed oil in the N.F. When the fourth edition of the Swiss Pharmacopœia was published, I discovered that this authority describes this oil as "dark green and clear," and orders its preparation in a copper vessel. As you can convince yourselves from submitted specimens, an oil results with a beautiful rich dark green color. In place of a copper vessel any ordinary dish will answer if a few copper coins are added when the oil is infused.

Although color is said to be no criterion in pharmacy, I am fully convinced that the physician as well as the patient and customer will prefer such a beautiful preparation to one of a brownish-green or greenish-brown color. The psychological effects alone of such an elegant galenical will benefit the patient.

Last, permit me to direct your attention to the use of sesame oil in place of olive oil in the U.S.P. and N.F. Oleates, and quite especially if they are intended to be absorbed.

CONCLUSION AND SUGGESTIONS.

In conclusion I want to emphasize the fact that I have no commercial interests whatsoever in sesame oil. The reason that I am so much in favor of this oil is that through years of experiment I am fully convinced from the practical as well as the scientific point of view that oleum sesami deserves admission into galenical preparations of the U.S.P. IX and N.F. IV.

I sincerely hope that in the resulting discussion a great many valuable points will be brought out and also that some of the members of the N. Y. State Pharmaceutical Association will give sesame oil a trial, report their experiments, and thereby be helpful to the U.S.P. and N.F. Revision Committee.

PROGRESS IN PHARMACY.

By M. I. Wilbert, Washington, D. C.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

(*Concluded from page* 450.)

Buchu.—E. M. Holmes reports a new adulterant of buchu which he has recognized as the leaflets of *Psoralea obliqua,* E. Mey, a small shrubby plant, 2 to 4 feet high, common near Stellenbosch, about 25 miles east of Cape Town, and therefore in the district where *Barosma betulina* grows (*Pharm. J.,* London, 1910, p. 69).

Cactina and Cactin.—E. P. Lyon and Guy L. Qualls report a series of experiments and observations on the influence of these substances on animals and on the pulse-rate and blood pressure in man. No effects were discoverable from the use of either cactin or cactina.

An editorial in calling attention to the report points out that the lavishness with which the two substances are being advertised would appear to indicate that they are still widely used and concludes that as a central theme for a treatise on the "Psychology of Advertising" these products may have their uses, they certainly illustrate the credulity of many otherwise well balanced medical men (*J. Am. M. Ass.,* 1910, v. 55, pp. 455–459 and 508).

Digitalis.—An editorial commenting on the proposed Government supervision of the standardization of digitalis, as suggested by Schmiedeberg, points out that this recommendation would virtually take the drug beyond the control of pharmacists, and questions the advisability of having a Government department acting as custodian of the drug (*Chem. and Drug.,* Lond., June 18, 1910, v. 76, p. 50).

New Digitalis Preparation.—A patent, issued to Tambach and Knoll, provides for the making of a preparation of digitalis which is to embody all of the activities of the fresh drug. The preparation is made by treating an alcoholic extract of the drug with ether, removing the resulting precipitate, concentrating the filtrate, and mixing the residue with milk sugar (*Pharm. Post,* Wien, 1910, v. 43, p. 502).

ERGOT.—Gordon Sharp presents an interesting historical study of ergot, its origin, botany, and chemistry. Under the latter heading he reviews, at some length, the more recent work on the chemistry of ergot and concludes with a review of the toxicology, pharmacology and therapeutics of the drug (*Pharm. J.*, Lond., 1910, v. 85, pp. 38 and 68).

Barger and Dale report the isolation of an active principle from ergot extracts which they believe to be the substance responsible for the intense activity exhibited by some ergot extracts in producing contraction of the isolated uterus of the cat. The relative abundance of this principle in dialysed extracts suggested that it was wholly or partly produced by micro-organisms and this supposition was confirmed by physiological experiments (*Pharm. J.*, London, 1910, v. 30, p. 757).

METHYL ALCOHOL.—George Arends believes it would be justifiable to investigate further the possibility of using purified methyl alcohol as a solvent for pharmaceutical preparations that are to be used externally. While he admits that the available literature is strongly against the use of this solvent at the present time, he appears to feel that much of the available evidence is misleading and that the reported deleterious results may be due entirely to the contaminating materials found in the commercial wood alcohol (*Pharm. Ztg.*, 1910, v. 55, p. 588).

The above suggestion has been vigorously opposed in Germany as being fraught with possible danger and it has been pointed out that the bulk of the available evidence would appear to indicate that even chemically pure methyl alcohol is dangerous. Until this evidence has been shown to be fallacious it would, of course, be inadmissible to use methyl alcohol as a solvent in any medicinal preparation.

MEXICAN JALAP ROOT.—E. M. Holmes points out that the French, German, Danish, and United States Pharmacopœias each requires that jalap yield 7 per cent. of resin, while the Belgian and Dutch Pharmacopœias require 8 per cent. He asserts that recently jalap assaying as high as 17 per cent. of resin has appeared on the London and Hamburg markets and attributes the improved quality to the unusually high price. He maintains that a good market price is almost certain to lead to a supply of good quality and that a price that will not pay the collector will depreciate the quality of any drug (*Pharm. J.*, London, 1910, v. 30, p. 789).

NUCLEIN, NUCLEIC ACIDS, AND NUCLEATES.—A general article describing these compounds has been prepared by the Council on Pharmacy and Chemistry for publication in N.N.R.

These products have been more or less widely used but their true value is as yet undetermined and many capable observers are inclined to think that the claims that have been made for the therapeutic value of these compounds are not based on sound conclusions (*J. Am. M. Ass.*, 1910, v. 55, p. 503).

OIL OF ROSE.—An editorial asserts that this year an unusual variety of adulterants have been put in the stills in the manufacture of otto of rose in Bulgaria and cautions the buyers to be on their guard (*Chem. and Drug.*, London, July 30, 1910, p. 149).

PODOPHYLLUM RESIN adulterated with aloes is reported by Joseph H. Williams who found approximately 25 per cent. of powdered aloes in a sample of resin of podophyllum which came within the limits of the tests prescribed by the Ph. Brit. IV. Williams thinks it would be advisable to apply tests for water soluble material in resin of podophyllum (*Pharm. J.*, London, 1910, v. 30, p. 608).

PUMPKIN SEED AS A VERMIFUGE.—H. H. Dale reports a pharmacologic study of pumpkin seed. He finds that neither the expressed oil nor the resin exert any anthelmintic or other physiological action. He holds that any value that the seeds may possess when administered in substance must be attributed solely to mechanical action.

In a further contribution Power and Salway report that they have failed to find any alkaloid, glucoside, or other definite compound likely to possess therapeutic action (*Pharm. J.*, London, 1910, v. 30, p. 703).

QUININE AND UREA HYDROCHLORIDE is being used quite widely as a local anæsthetic. In a recent number of the *Journal of the American Medical Association* (June 11, p. 1940), W. O. Green reports 4 cases in which the substance was used with apparently satisfactory results.

QUININE ARSENATE.—The Council on Pharmacy and Chemistry of the American Medical Association reports that quinine arsenate was submitted to the staff of clinical consultants and, on their recommendation, refused recognition in New and Non-official Remedies because it does not appear that this preparation possesses any properties that may not be found in a simple mixture of its components. Attempts to substitute it for other quinine salts would

lead to overdosing with arsenic (*J. Am. M. Ass.*, 1910, v. 55, p. 235).

SCOPARIUS.—J. Chevalier reports a systematic study of the sparteine content of scoparius at different seasons of the year. For the whole plant the highest, 0.68 per cent., was found in March. This rapidly decreases, being but 0.325 per cent. in April. The minimum is reached in August, 0.233 per cent., and from this a gradual rise to November with 0.475 per cent. The dried and ripe fruit was found to have 1.10 per cent. of sparteine (*Apotheker Ztg.*, 1910, v. 25, p. 466).

SCOPOLAMINE.—Delbet and Dupont warn against the use of scopolamine for general anæsthesia; their review of 120 cases includes 2 fatalities, one serious post-operative syncope, and a number of other mishaps (*J. Am. M. Ass.*, 1910, v. 55, p. 257).

SPRITOL is the name given to a substitute for ethyl alcohol that on examination was found to consist of wood alcohol (*Apoth. Ztg.*, Berlin, 1910, v. 25, p. 136).

VIROID.—Dr. Henry Freeman Walker suggests the word "Viroid" as a generic term for designating the biologic specifics used in active immunization. He believes that this name would be distinctive in that it would indicate, with the necessary prefix, the virus for which it would be used as an antidote. It would also restrict "Vaccine" to the now well-established cow-pox virus (*J. Am. M. Ass.*, 1910, v. 55, p. 42).

DRUGS.—J. Biberfeld (*Deut. Med. Wchnschr.*), in a review of the pharmaceutical harvest of the last few years, asserts that not much grain is left after separating it from the chaff (*J. Am. M. Ass.*, 1910, v. 55, p. 541).

AN ALKALOIDAL SYNTHESIS.—Pictet and Finkelstein ("Berichte," xlii, 1979) have succeeded in synthesizing the alkaloid laudanosine (methyl-tetra-hydro-papaverine) by the interaction of homoveratrylamine and homoveratric acid. The latter body is prepared from eugenol by the method elaborated by Tiemann and Matsmoto (*Chem. and Drug.*, London, July 30, 1910, p. 159).

FLUIDEXTRACTS.—An interesting and timely contribution to the preparation and valuation of galenical preparations is presented by the chief apothecary of the city hospital, Berlin, H. Linke.

He reviews the introduction of fluidextracts in the German Pharmacopœia, the expectations that were expressed twenty years ago, and the failure of these expectations to materialize on account

of the difficulties involved in the production of these preparations.

In common with other observers he notes that the complete exhaustion of a drug requires from 5 to 8 times the weight of the drug itself. He also discusses the economic questions that are involved in the production of fluidextracts by manufacturers, the variation in the price of the preparations, and presents a table giving the results of his observations on a number of commercial preparations and an equal number made in the laboratory of the hospital with which he is connected (*Apoth. Ztg.*, Berlin, 1910, v. 25, pp. 522–523).

MELTING POINT DETERMINATION.—L. Derlin recommends the metallic bath as being the most satisfactory for determining the melting point of most organic chemicals used in pharmacy. For substances that melt at higher temperatures the figures are usually low (*Apotheker Ztg.*, 1910, v. 25, p. 435).

Richter Ernst, in discussing the value of melting point determinations, points out the advantage of the apparatus figured in "*Vierteljahresschrift für praktische Pharmazie*, 1907, p. 145. This apparatus has the advantage that the sulphuric acid circulates and heats evenly so that the apparatus can be allowed to stand without further care. To prevent the destruction of the cork he recommends coating it with collodion (*Apotheker Ztg.*, 1910, v. 25, p. 476).

REFRACTOMETER.—The *Chemist and Druggist*, July 16, 1910, p. 51, points out that the next edition of the British Pharmacopœia will probably provide refractive indices for oils and other liquids the quality of which may be determined by examination with the refractometer, an instrument whose value in the examination of essential oils is well established. The article includes a description and illustration of the refractometer generally used.

ARBEITEN AUS DEM PHARMAZEUTISCHEN INSTITUT DER UNIVERSITAT BERLIN.

Of the large number of papers appearing in the annual publication of the work done at the Pharmaceutical Institute of the University of Berlin, none are so important and of such practical value as those which reveal to physicians and pharmacists the false and misleading claims, to say nothing of downright sophistication, made in the

manner of introducing and exploiting many of the so-called newer remedies.

This work of investigation done by the Institute is in line with the effort made by the American Medical Association and so fruitfully carried out by its Council on Pharmacy and Chemistry to inform the physicians of this country how they have so successfully been preyed upon and used by unscrupulous manufacturers.

When one reads of such conditions in other countries, it is apparent that credulity and gullibility are not confined to these United States. It must be exceedingly gratifying to those who are hopeful of better things that there are some men who are both able and willing to do the painstaking analytical work required to determine the truth about remedies intended for the sick, and tell the truth about them without fear or favor. It is only by the greatest possible publicity, in this as other lines of work, that those who desire to profit "by ways that are dark and devious," can be restrained and curbed and made to be honest.

The following abstracts were prepared from the annual publication edited by Dr. K. Thoms, Director of the Institute.

An Adulterated Acetylparamidosalol.—In the Pharmacopœia Helvetica IV, acetylparamido phenolum salicylicum is the scientific name for salophen. A careful examination by Zermik, of the contents of an original package labelled acetparamidosalol showed it to be a mixture of 75 parts of the original and 25 parts of acetanilid.

Eulatin.—A white, odorless, slightly sour-tasting powder, which the manufacturers claim to be a true chemical compound and termed by them amidobrombenzoic acid dimethylphenylpyrazolon.

Friedmann, in the *Med. Klinik,* 1908, states that it is of use in whooping-cough, that it promotes expectoration, and diminishes the frequency and intensity of the spasm in this disease.

Zernik gives in detail his analysis of the contents of an original package bought on the open market. He found it to be a white, crystalline powder of a bitter taste, slightly soluble in water and completely soluble in alcohol, particularly on warming. The solution gave an acid reaction and a clear violet fluorescence. At 75° eulatin began to liquefy and at 150° it had completely melted. On crystallizing some of the preparation from alcohol, a needle-shaped crystalline body with a constant melting point of 251°–252° was obtained. This behavior signified to him that eulatin must be a

mixture and this assumption was confirmed by the following experiments.

Five-tenths of a gramme of eulatin was mixed three times with 10 c.c. of cold water and after standing a short time the combined solutions were filtered. In the faintly violet fluorescent solution antipyrine was demonstrated in the usual manner; on the other hand, the undissolved residue contained no antipyrine, but showed a melting point of 251°.

Five-tenths of a gramme of eulatin was treated in a like manner three times with 10 c.c. cold benzol; the undissolved residue was free of antipyrine and melted at 251°.

It, therefore, became necessary to identify this substance with the melting point of 251°. Literature contains not less than six isomers of amidobrombenzoic acid, the highest melting point being 225°. The foregoing substance proved to be soluble in and lost its acidity in sodium carbonate solution. Several grammes of finely powdered eulatin were shaken in a separatory funnel with a mixture of chloroform and sodium carbonate solution until completely dissolved. The lower chloroformic layer was drawn off and the alkaline solution shaken out twice again with chloroform. The combined chloroformic solutions, on evaporation, left a residue of pure antipyrine, melting point 109°–111°. The alkaline solution was treated with dilute H_2SO_4 to liberate the acid, which was recrystallized from toluol; melting point 251°–252°.

The crystallized substance gave a negative result with Lassaigne's reagent, showing the absence of nitrogen and therefore of amidobrombenzoic acid, although bromine was found in the substance. A determination for bromine, by the method of Carius, of 0.2690 Gm. of the substance, gave the following result, 0.2520 Gm. AgBr = 39.87 per cent. Br.

Literature records a brombenzoic acid with a melting point of 251° known as p-brombenzoic acid.

A mixture of the acid obtained from eulatin and pure p-brombenzoic acid showed a melting point of 251°. Besides p-brombenzoic acid eulatin contained still another acid.

On shaking the acid filtrate from the p-brombenzoic acid with ether, a nitrogen body (but free from bromine), acid-like in character, was extracted. It had a melting point of 144°–145° and proved to be o-amidobenzoic acid (anthranilicacid). A mixture of this with pure o-amidobenzoic acid showed no difference in melting point.

Zernik claims that p-brombenzoic acid is only a mechanically mixed ingredient in eulatin, and that it is hard to believe that o-amidobenzoic acid is chemically bound to the antipyrine. At least the following experiment is evidence against it. If eulatin is extracted with cold, absolute ether, p-brombenzoic acid, o-amidobenzoic acid, and antipyrine go into solution. If the ethereal solution is shaken out with cold water the antipyrine is obtained, while the acids remain in solution in the ether.

It was further ascertained that when eulatin is subjected to a temperature of 100° it loses by weight 0.56 per cent., and when shaken out with chloroform 50.94 per cent. antipyrine is separated.

As a result of his calculations he states that it is a mixture of two parts of p-brombenzoic acid and antipyrine in molecular proportions and one part o-amidobenzoic acid and antipyrine, also in molecular proportions. He says that it is impossible to determine by analytical means just how this mixture is brought about. The declaration that eulatin is "amidobrombenzoësaures antipyrine" he states to be untrue according to his investigation.

Physicians should be very careful, he advises, in accepting recommendations and testimonials of the many preparations of supposedly newer composition on the market.

Meligrin.—The makers of this product give no information as to its true nature. A microscopical and chemical investigation by Zernik of the contents of an original package bought on the open market showed it to be a mixture of 86 parts of antipyrine and 14 parts of methylacetanilid (exaligin).

It is a white crystalline powder, very soluble in water, with the bitter taste characteristic of antipyrine.

The manufacturers of this remedy have taken advantage of the fact that antipyrine (like sodium salicylate, chloral, etc.) increases the solubility in water of many organic substances.

Mergandol is the name given to a liquid preparation recommended for intramuscular injection for the treatment of syphilis and also for external application on the skin eruptions of the same disease.

The manufacturers state that it is a solution of hydrargyrum-natriumglyceratum in glycerin, each cubic centimetre containing 0.0035 pure mercury.

Zernik says that while sodium glycerate is mentioned in chemical literature, mercury or mercury-sodium glycerate is unknown.

An examination of an original bottle showed it to be a colorless, syrupy liquid of a neutral reaction, specific gravity 1.2177 at 15°. A qualitative analysis showed the presence of glycerin, mercury, sodium, and chlorine. Further quantitative determinations showed that in 100 c.c. of the liquid there were present 0.4944 per cent. of mercuric chloride and 0.9269 per cent. of sodium chloride.

It is conclusively proven by Zernik that mergandol is a solution of these two salts in glycerin and water and not a solution of quicksilver-natrium-glycerates in glycerin.

Phagocytin.—Under this name there has appeared on the German market a sterile solution, recommended by the exploiters for subcutaneous injection in septic and exhausting diseases. It is dispensed in ampouls each containing, so the label stated, one cubic centimetre of a 5 per cent. solution of, what the makers claim, sodium nucleinate.

At the request of the Deutschen Apothekervereins the Pharmaceutic Institute undertook an investigation of this preparation.

It was marketed in cartons of twenty ampouls each. The ampouls contained a brownish liquid of an alkaline reaction; upon the addition of a mineral acid a white, flocculent precipitate was formed.

Each ampoul contained somewhat more liquid than the quantity stated on the label.

Upon evaporation of one cubic centimetre of the liquid there remained a brown, amorphous residue which, after drying at 100°, weighed 0.054 gramme, somewhat more than stated on the label.

On heating the residue to ash there developed the characteristic odor of garlic, which led the analyst to suspect the presence of arsenic; this suspicion was later confirmed by positive results with Marsh's and Bettendorf's tests.

In the original solution the presence of arsenic could not be demonstrated in the usual manner. Only after destruction of the organic substance was its presence confirmed by the above tests; it was also precipitated as sulphide with hydrogen sulphide.

The ash of phagocytin showed further the presence of sodium, besides traces of potassium and iron, combined with carbonic, phosphoric, and sulphuric acid.

Further quantitative determinations showed that phagocytin was a 5 per cent. solution of an organic combination of arsenic.

Plejapyrin.—The introducers of this remedy speak of it as being

a very soluble and ideal migraine powder of true chemical combination obtained by the condensation of molecular portions of benzamid and phenyldimethylpyrazolon. They also claim that it can be administered in one gramme doses several times a day, is well borne, and without any untoward after-effects.

A chemical and microscopical examination of an original package of the powder showed it to be merely a mechanical mixture of antipyrine and benzamid. This was later confirmed by mixing antipyrine and benzamid in molecular proportions and subjecting the mixture to the same method of analysis as applied to the original. The results were absolutely the same.

Plejapyrin has been withdrawn from the market.

Pyrenol.—In the *Apotheker-Zeitung*, Number 100, 1907, Zernik publishes the result of his analysis of the above-named preparation, and states positively that instead of being a definite chemical compound, as claimed by the manufacturers, it is simply a mixture of well-known chemicals. He also states that the constitutional formula given by the maker is scientifically impossible.

The manufacturer, in a written communication to the Institute, takes exception to Zernik's findings and reiterates that pyrenol is not a mechanical mixture but a true chemical combination which he terms "benzoësäurethymolester benzoyl-oxybenzoësäure neutralized with sodium."

At the request of Dr. Thoms, Professor Gadamer, director of the Pharmaceutical Institute of the University of Breslau, had his assistant Dr. Gaebel undertake and carry out a series of experiments and complete analysis of an original package of pyrenol.

Dr. Gaebel gives in detail each step of his investigation, and concludes by stating that pyrenol is a mechanical mixture of equal parts of sodium salicylate and sodium benzoate with 1 per cent. of benzoic acid and not more than 0.3 per cent. of thymol.

This result practically confirms Zernik's investigation and was in turn confirmed by an exhaustive analysis made by Dr. Thoms himself.

JOHN K. THUM.

CORRESPONDENCE.

EDITOR AMERICAN JOURNAL OF PHARMACY.

Dear Sir: Your attention is called to the action of the Indiana Board of Pharmacy with a view to its publication in the interests of pharmaceutical education.

The influence of the syllabus is apparent and its bringing of the schools and the boards together is not one of the least of its purposes.

The criticism that the amount of work should require more than 1000 hours is one that is uniformly made by those that give close consideration to the subject, but the facts should be recalled that the campaign for even 1000 hours was long and arduous and that many have not fully recovered from the effects of this standard.

"The Indiana Board of Pharmacy at its meeting on the 14th of this month (July) called a conference of all the schools of pharmacy in the State, each of which sent a representative. After a lengthy discussion the schools with the Board of Pharmacy adopted the syllabus as the standard.

"The criticism of all was that the standard was rather low and that the amount of work should require more than 1000 hours."

The Regents on the recommendation of the New York State Board of Pharmacy advanced the requirements in New York State to 1100 hours, 500 recitations and 600 laboratory.

Handbook No. 11 entitled Pharmacy has just been printed by the Department and copies may be secured without expense on application to the Education Department, Albany, N. Y. It contains the new law, the rules of the Board, notes on the law, the schools registered by the Regents or accredited by the Department, and the synopsis showing the statutory requirements for the practice of pharmacy throughout the United States.

Chairman Engstrom of the Chemistry Branch of the Syllabus Committee has addressed a letter to his subcommittee for suggestions of improvement.

He calls attention to the incomplete character of the work and the criticisms that have reached him.

The pharmaceutical press will confer a favor on the Executive Committee by calling attention to any suggestions, corrections, or discussions that appear in its columns. The letter head gives the names and addresses of the members of the Executive Committee.

Respectfully yours, H. L. TAYLOR.

ALBANY, N. Y., August 1, 1910.

BOOK REVIEWS.

ALLEN'S COMMERCIAL ORGANIC ANALYSIS. Vol. III. Fourth Edition, entirely rewritten. Edited by W. A. Davis and Samuel S. Sadtler. Philadelphia, P. Blakiston's Son and Co., 1012 Walnut St., 1910. $5.00 net.

In this volume a number of subjects are considered, each having been prepared by special contributors. The chapter on "Hydrocarbons" was written by F. C. Garrett, of New Castle-upon-Tyne, England. The parts on "Bitumens," "Phenols," and "Anthracene and its Associates" were prepared by S. S. Sadtler, of Philadelphia. The monographs on "Naphthalene and its Derivatives" and "Phthalic Acid and the Phthaleins" were written by W. A. Davis, of London. The chapter on "Aromatic Acids" is the work of Edward Horton, of London. "Gallic Acid and its Allies" received the special attention of W. P. Dreaper, of London, and the monograph on "Modern Explosives" was written by A. Marshall, of Naini Tal, India.

While all of the volumes of "Allen's Commercial Organic Analysis" are of interest and value, this one will be of particular interest to pharmacists, as it treats of so many of the compounds that are used either directly or indirectly in medicine. The information given concerning cresols, creosote, creosote oils, phenol, benzoic acid, cinnamic acid and its derivatives, aromatic balsams, cinnamic balsams, salicylic acid and its allies, etc., is extremely valuable. The good features which were noted in the review of Volumes I and II (this JOURNAL, August, p. 381) apply with equal force to Volume III. Finally, it should be noted that in the editorial work of this volume Mr. Sadtler has been associated with Mr. Davis. Professor Leffmann having found it impossible to continue as American editor of the series and at the same time prepare those articles for which he has become responsible, his editorial work will in the future be assumed by Mr. Sadtler.

A TEXT BOOK OF ORGANIC CHEMISTRY. By Prof. William A. Noyes, University of Illinois. Second Edition, Revised. New York: Henry Holt and Company, 1910.

This is one of the best elementary books on "organic chemistry" that has been published. The present edition will be of special interest to pharmacists and physicians, as the chapter on

"Compounds of Interest in Physiology and Pathology" has been rewritten on the basis of the classification of proteins, recently adopted by the American Society of Biological Chemists and the American Physiological Society. A number of other changes and additions have been made.

NORMAL HISTOLOGY, with Special Reference to the Structure of the Human Body. By Prof. George A. Piersol, University of Pennsylvania. 438 illustrations, many of which are in colors. Eighth Edition (Rewritten). Philadelphia and London: J. B. Lippincott Company.

It is indeed gratifying that the medical student has such an excellent text-book on histology as the one in hand. It is well arranged, well written, and profusely illustrated, not only with histological material showing microscopic details, but in some instances with the macroscopic material, as of the human brain, showing the gross anatomy of this organ and the relation of the different parts to each other.

The book comprises over 400 pages and includes chapters on the cell, the elementary tissues, the blood vascular system, the lymphatic system, mucous membranes and glands, the alimentary canal, the organs of respiration, the urinary organs, the male reproductive organs, the female reproductive organs, the central nervous system, and the sense organs. There is also an excellent chapter on microscopical technic.

Much of the work that is here given should be followed by the pharmacist, who engages in the examination of blood, urinary sediments, and other pathological products, and it would seem advisable if hygiene, as now taught in colleges of pharmacy, could be made an entrance requirement, and the time given to this subject at college replaced with some work on the normal histology of the human body.

THE NEW STANDARD FORMULARY. Comprising in Part I all preparations official or included in the Pharmacopœias, Dispensatories, or Formularies of the world, together with a vast collection from other sources. The parts following embracing Domestic and Veterinary Remedies, Proprietary and Synthetic Remedies, Perfumes and Toilet Articles, Soda and other Beverages, and Domestic Utilities. By A. Emil Hiss and Albert E. Ebert. Chicago: G. P. Engelhard and Company, 1910.

The present volume has been so extensively revised and greatly enlarged that it is more than double the size of the original Standard Formulary. Each primary topic as "Abstracts" has an introductory paragraph which will be found helpful in making those preparations of a given class where formulas may not be given.

The book represents an immense amount of work, not only in collating the information, but in editing, and so far as we have been able to determine has been exceptionally well done. It will be found indispensable to pharmacists and manufacturers.

THE EXTRA PHARMACOPŒIA OF MARTINDALE AND WESTCOTT. Revised by W. Harrison Martindale and W. Wynn Westcott. Fourteenth Edition. London: H. T. Lewis, 136 Garver St., W. C., 1910.

Owing to the introduction of a large amount of new matter the form of the "Extra Pharmacopœia" has been slightly changed, the size of the page of the present volume being 6⅝ x 4½ inches. There are new chapters upon Acidi Lactici Bacilli, Organic Arsenic Compounds, Iontaphoresis, Radium, etc. About 100 additional patent and proprietary medicines are described.

In a special volume forming an Addendum to the "Extra Pharmacopœia" is a chart for the recognition of organic chemical bodies used in therapeutics. In this are given facts regarding the solubility, effects of reagents, heat, etc., upon over 300 different substances.

DIGEST OF COMMENTS ON THE PHARMACOPŒIA of the United States of America (Eighth Decennial Revision) and the National Formulary (Third Edition) for the Calendar Year ending December 31, 1907. By Murray G. Motter and Martin I. Wilbert. Washington: Government Printing Office, 1910.

This is the third volume of "Digest of Comments" edited by Dr. Motter and Mr. Wilbert and published under the direction of the Surgeon-General of the Public Health and Marine-Hospital Service of the United States, and constitutes Bulletin No. 63 of the Hygienic Laboratory. It is exceedingly gratifying that these volumes are appearing with the rapidity that they are, as the references are more complete and the abstracts more satisfactory than in any other publication available. The favorable comments which have been made in this JOURNAL regarding the previous Bulletins relating to "Digest of Comments" apply to this volume in hand.

The wisdom of the Board of Trustees of the U. S. Pharmacopœial Convention (1900), in effecting the co-operation of the Surgeon-General of the Public Health and Marine-Hospital Service of the United States in this work, is becoming more and more apparent as each volume of "Digests" appears.

THE ORGANIZATION OF ILL-HEALTH.

There are a number of commercial interests in this country that do not want an independent national department of health. In recent years we have had many exposures of the patent medicine swindle. We have learned that most of the most popular patent medicines, the so-called tonics, were nothing more than dilute alcohol with certain bitter drugs so as to make them taste mediciny. Physicians have seen alcohol habits formed as a consequence of freely imbibing these alcoholic preparations. Some of them were meant particularly for women's diseases, and the consequence has been a feminine nipping at alcoholic products that has worked serious harm to the women of the country. We have also found that the headache powders so commonly advertised were composed of drugs which, when taken as freely as was advised on the labels of many of these preparations, were seriously dangerous. We have had not a few, but many, deaths as a consequence of them. The soothing syrups for children mostly contained opium and were seriously injuring the growing child at an important period of its development, and adding to the number of nervous wrecks with tendencies to drug addictions in after life that we had in this country.

For a time after these exposures the patent medicine swindlers were very quiet. In many cases their advertisements disappeared from their usual places. Now they are gaining courage again. The American people have proverbially a very short memory for such exposures. The patent medicine people dread very much the organization of a national department of health, because this will sadly interfere with their now happy prospect of reviving their business and fattening their purses at the cost of the health of our people. This is one element in the opposition organized for ill-health.

There are others. There are a number of people in this country who would like to be freer to foist drugs, impure foods, and ques-

tionable products of many kinds on our inhabitants, so as to make money, cost what it might in the health of those who consumed them. The consumer's purse they are interested in, but not his health. The organization of the national Bureau of Health, with its strict enforcement of the Pure Food and Drugs Act, and its sure tendency to further protect by legislation the health of our people, is a dread spectre to such exploiters of the public, and, of course, they want to lay it if possible.

The League for Medical Freedom has a rallying cry. It is that the doctors are trying to create a medical monopoly—a doctor's trust. They insist that the Owen bill is due to the American Medical Association. As a matter of fact the bill emanates from the Senator from Oklahoma himself, and the movement for a national department of health has been organized, not by the American Medical Association, but by the Committee of One Hundred of the American Association for the Advancement of Science. This organization, as is well known, consists not of physicians, but of the united scientists of the country, and only a very small proportion of physicians are in the membership. The Committee of One Hundred contains the names of many of the representative thinking citizens of this country. They come from all over the country. It is absolutely absurd to talk about such men as organizing a medical trust. Practitioners of all the different cults in medicine are agreed that a national department of health would be a good thing, and cannot possibly interfere with present State laws as to medical practice. This organization of opposition should of itself be a strong argument for the Owen bill. We have the Organization of Ill-Health for commercial reasons. Let us recognize and appreciate at their true value exactly the elements that are engaged in it. —*The Independent;* reprinted from *Science,* July 15, 1910, pp. 84, 85.

PROFESSOR CHARLES F. CHANDLER.

Professor Chandler, who has been the Professor of Chemistry in the College of Pharmacy of the City of New York since 1866, delivered a farewell address to the members of that college on Tuesday evening, March 15, 1910, and at a testimonial dinner tendered to Professor Chandler by the officers, trustees, faculty, and members,

and the Alumni of the college at the Hotel Astor on March 28, 1910, a beautiful silver loving cup was presented to Dr. Chandler and the following resolutions were adopted:

WHEREAS

CHARLES F. CHANDLER,

A.M., PH.D., M.D., LL.D., D.SC.,

during the forty-three years of his connection with this college, has by his constant earnest work for the increase of its educational facilities contributed in a large degree to its advancement from a small school of pharmacy to a department in Columbia University, and

WHEREAS, As Professor of Chemistry and Professor of Organic Chemistry, he has shown in his lectures a masterly delivery and a wealth of illustration that have commanded the respect and esteem of his classes and made each student a personal and enthusiastic friend; therefore be it

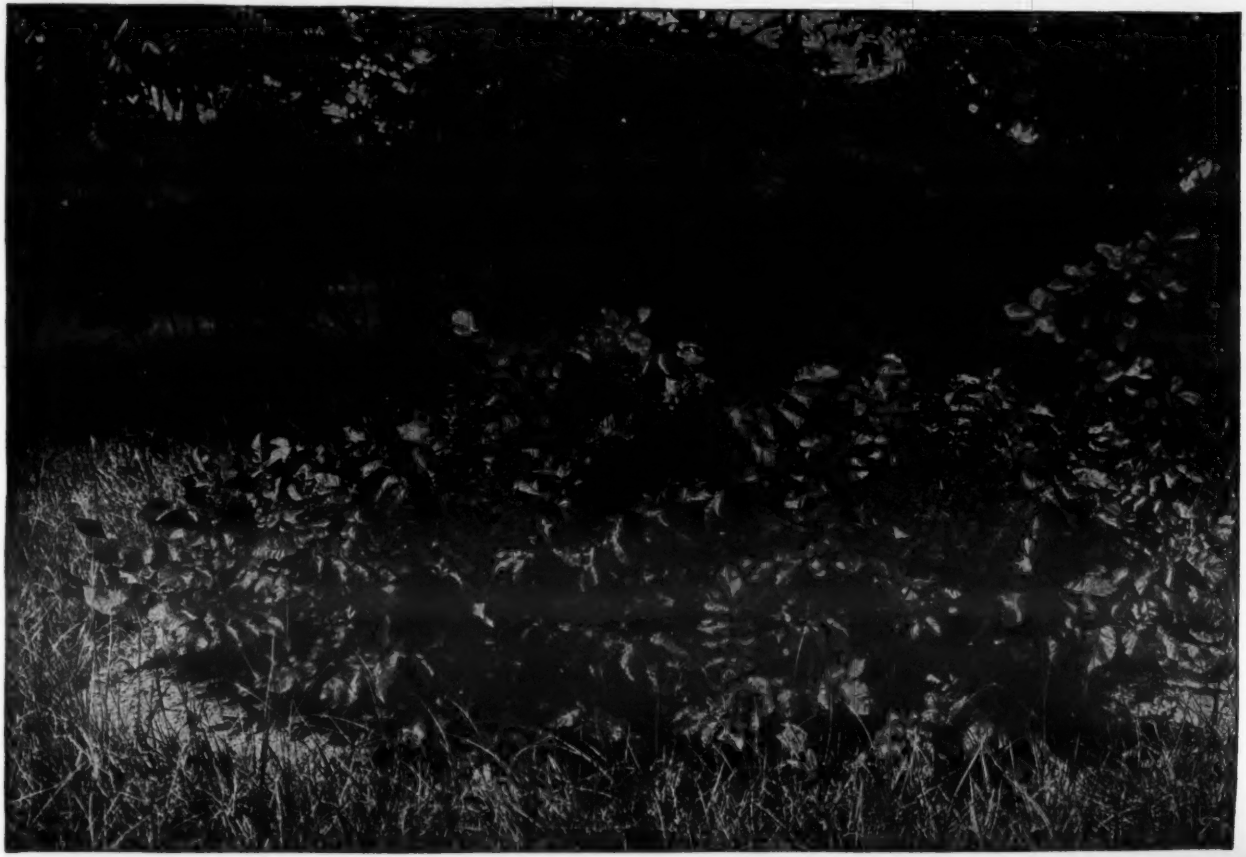
Resolved, That we hereby express our high appreciation of his distinguished services to the institution, our regret that he wills at this time to retire from its faculty, with our earnest hope that he may for many years enjoy the love and esteem of his hosts of friends, and the well-earned honors universally conceded to his eminence in the profession to which his life has been devoted. And be it further

Resolved, That these resolutions be spread in full upon the college records and a copy suitably engrossed be presented to him.

A testimonial dinner was also tendered Dr. Chandler by his former students and associates of the faculty of Columbia University at the Waldorf-Astoria on April 2, 1910.

The chemists of America, including The Chemists' Club, The Society of Chemical Industry, The American Chemical Society, The American Electro-Chemical Society, The American Institute of Chemical Engineers, and The Verein Deutscher Chemiker tendered Dr. Chandler a banquet at the Waldorf-Astoria on April 30, 1910.

The resignation of Dr. Chandler, after nearly fifty years of efficient and devoted service, has elicited such a spontaneous outburst of appreciation and affection from his former students, colleagues, and fellow-scientists that it was deemed appropriate and desirable that a permanent record should be made of the several banquets tendered to Dr. Chandler by his friends and to enumerate and describe the testimonials presented to him. These are published in a "Testimonial Supplement" of the *Columbia University Quarterly* of June, 1910.



DWARF SUMACH, RHUS MICHAUXII.